PREPARATION OF SUBSTITUTED CYCLOPENTANE AND CYCLOPENTENE COMPOUNDS AND CERTAIN INTERMEDIATES

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DESCRIPTION

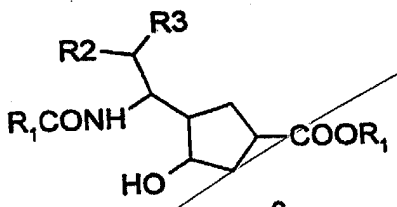
Technical Field

This invention relates to methods for preparing certain substituted cyclopentane compounds and certain intermediates thereof. The present invention is also concerned with novel intermediates or precursors for producing the substituted cyclopentane compounds. Substituted cyclopentane compounds prepared according to the present invention are useful as neuraminidase inhibitors, and especially in pharmaceutical composition for preventing, treating or ameliorating viral, bacterial and other infections.

Background of the Invention

Despite the wealth of information available, influenza remains a potentially devastating disease of man, lower mammals, and birds. No effective vaccine exists and no cure is available once the infection has been initiated.

Influenza viruses consist of eight pieces of single stranded RNA, packaged in orderly fashion within the virion. Each piece codes for one of the major viral proteins. The replication complex is enclosed with a membrane composed of matrix protein associated with a lipid bilayer. Embedded in



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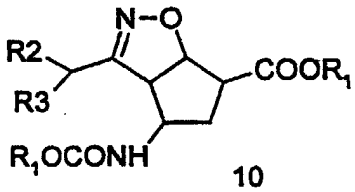
converting the alcohol group of said acylated compound into a leaving group;

displacing said leaving group with ammonia or guanidine to obtain said compound of formula 1a; or displacing said leaving group with an azide ion and then converting to a guanidine with a NH_2 compound to obtain said compound of formula 1a.

~~4. A method for preparing isoxazoline compounds~~ represented by the formula 10:



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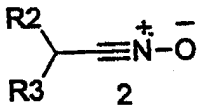
wherein each R_1 individually is alkyl or substituted alkyl, alkenyl or substituted alkenyl of 1-6 carbon atoms, or H; each of R_2 and R_3 individually is alkyl or alkenyl of 1-8 carbon atoms, cycloalkyl or substituted cycloalkyl of 4-8 carbon atoms, aryl or substituted aryl, arylalkyl or substituted arylalkyl, or H provided at least one of R_2 and R_3 is other than H;

which comprises reacting a nitrite oxide of formula 2



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with a cyclopentane derivative ~~of the~~ having formula 9

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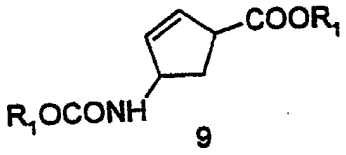

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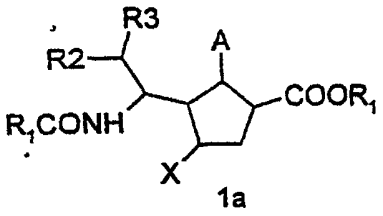
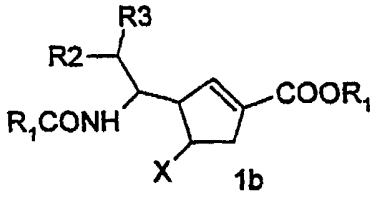
to produce said isoxazoline compound.

5. A method for preparing a substituted cyclopentane compound represented by formulae 1a or 1b



1a



1b

wherein each R_1 individually is alkyl or substituted alkyl, alkenyl or substituted alkenyl of 1-6 carbon atoms, or H; each of R_2 and R_3 individually is alkyl or alkenyl of 1-8 carbon atoms, cycloalkyl or substituted cycloalkyl of 4-8 carbon atoms, aryl or substituted aryl, arylalkyl or substituted arylalkyl, or H provided at least one of R_2 and R_3 is other than H; X is NHR_1, $NHC(=NH)NHR_4$ where R_4 is H, alkyl of 1-6 carbon atoms, OR_1, COR_1, $COOR_1$ CN or NO_2; A is H, F, OR_1, $OCOR_1$, $-OOCNHR_1$, NHR_1, or $NHCOOR_1$; and pharmaceutically acceptable salts thereof;

which comprises:

obtaining an isoxazoline compound ~~of formula 10 according to claim 4;~~

Improper dependency

Insert the rest of claim 4 here

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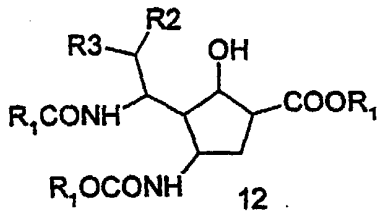
converting said isoxazoline to a compound of formula 12



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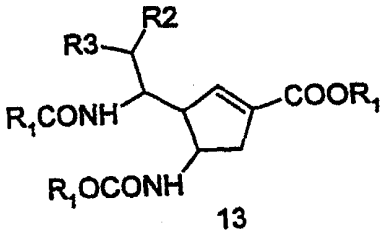
and dehydrating said compound of formula 12 to produce a compound of formula 13



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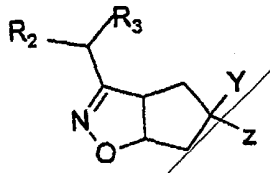
or converting the OH groups of said compound of formula 12

to a group selected from the group of F, OR, OCOR, NHR_1 or NHCOOR, except when said grop is OR_1, R_1 is other than H.

6. An isoxazoline derivative represented by the following formula 4:

Intermediate



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wherein each of R_2 and R_3 individually is alkyl or alkenyl of 1-8 carbon atoms, cycloalkyl or substituted cycloalkyl of 4-8 carbon atoms, arylalkyl or substituted arylalkyl, or H provided at least one of R_2 and R_3 is other than H; each of Y and Z individually is $COOR_1$ or H provided that at least one of Y and Z is other than H.